

REMARKS/ARGUMENTS

Applicants provide herewith an amendment to the claims as described above. Support for all amendments is found in the specification as originally filed, and is further discussed below. Applicants submit that no new matter has been added by way of the above amendment. Accordingly, entry of the amendment is respectfully requested.

The Office Action dated April 22, 2009, included claim rejections based on alleged lack of written description (35 U.S.C. § 112, first paragraph), and alleged anticipation (35 U.S.C. § 102). Applicants traverse all rejections to the extent that they may be applied to the amended claims, for the reasons noted below. The present Response with Amendment is fully responsive to each of the Examiner's points, and Applicants respectfully request reconsideration of the claims in view of the amendments and remarks herein.

THE STATUS OF THE CLAIMS

Claims 1-16 are withdrawn from further consideration.

Claims 17-26 are pending and are presently under examination.

Claims 27-61 are cancelled.

Claims 17, 19 and 26 are currently amended herein.

This amendment to the claims does not introduce new matter. These amendments are made without prejudice and are not to be construed as abandonment of any originally claimed subject matter or agreement with any objection or rejection of record. Support for the amended claims 17, 19 and 26 is found throughout the specification as originally filed, as shown, for example, below.

Claim Element	Location of Support (paragraph number)
a leucyl-O-tRNA comprising a nucleotide sequence of SEQ ID NOS: 1 and 2	See the response to the first office action (Response dated September 16, 2008).

Claim Element	Location of Support (paragraph number)
a leucyl O-tRNA comprising (i) an anticodon loop comprising a CU(X) _n XXXAA sequence, (ii) a first intramolecular base pair selected from U28:A42 and C28:G42, (iii) a second intramolecular base pair selected from G:49:C65 and C49:G65, and (iv) at least about 25% suppression activity in the presence of a cognate synthetase in response to a selector codon as compared to a control lacking the selector codon, and where the selector codon is a four-base codon	See paragraphs 0012, 0013, 0015, 0062, 0070-0073, 0081, 0106, 0128, 0171, and FIGS. 4 and 5.
a leucyl O-tRNA comprising an anticodon loop comprising (i) a CUUCAAA sequence, and (ii) at least about 25% suppression activity in the presence of a cognate synthetase in response to a selector codon as compared to a control lacking the selector codon, and where the selector codon is an opal codon	See paragraphs 0012, 0015, 0062, 0070-0073, 0081, 0106, 0128, 0171, and FIGS. 4 and 5.
an orthogonal aminoacyl-leucyl-tRNA synthetase (leucyl-O-RS) that comprises at least about 90% amino acid identity as a leucyl-O-RS of SEQ ID NO: 15 or 16	See paragraphs 0018, 0032, 0090 and 0147.

CLAIMS 17 and 26

In the Office Action dated April 22, 2009, the Examiner points out that SEQ ID NOS: 1 and 2, which were added in the Amendment that accompanied the Response filed on September 16, 2008, were not originally presented species. Applicants respectfully request the searching of these two species and their inclusion in the pending claimed subject matter.

Applicants have added generic embodiments of the claimed invention to pending claims 17 and 26. Applicants respectfully request the inclusion of these aspects in the pending claimed subject matter. Support for these aspects is found throughout the specification, as itemized in the table above.

35 U.S.C. § 112, FIRST PARAGRAPH

In the Office Action, claims 17-26 were rejected under 35 U.S.C. § 112, first paragraph, where the specification allegedly lacks sufficient support for O-tRNA/O-RS pairs in view of the O-RS genus allegedly lacking sufficient description to permit a user to determine what is included within the genus of O-tRNA/O-RS pairs without empirical testing to find a suitable O-RS species. The Examiner states that the O-RS can allegedly be of “any structure” as found in

claims 17 and 26. Further, the Examiner alleges that the O-RS molecules that are “conservative variants” or molecules with “50% suppressor efficiency” as recited in claims 18 and 19, respectively, do not remedy this lack of description and still do not provide sufficient guidance to construct a functional O-RS/O-tRNA pair.

Applicants respectfully disagree, and traverse this rejection. The O-RS molecules recited in claim 17 are sufficiently described by the language that appears in claim 17 in view of the teaching in the specification. Claim 17 requires that the O-RS preferentially aminoacylates the O-tRNA with the selected amino acid. This functional limitation is read in view of the content of the specification that teaches how to construct, identify and produce suitable O-RS molecules with a suitable structures that have this functional limitation.

However, solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner’s rejection, the Applicants have amended claims 17 and 26. Rebuttal to the Examiner’s rejection is made in view of the amended forms of claims 17 and 26.

The amended form of claim 17 requires that the leucyl-O-RS comprises at least about 90% amino acid identity with a leucyl-O-RS of SEQ ID NO: 15 or 16. This high degree of amino acid sequence conservation, in combination with knowledge of O-RS secondary structure and active site conformation as known in the art (for example, as described in paragraphs 0191, 0192 and 0201-0206) clearly defines what can be included in a genus of suitable O-RS molecules.

Similarly, the amended form of claim 26 is now limited to leucyl-O-RS species comprising at least about 90% amino acid identity with a leucyl O-RS derived from *Methanobacterium thermoautotrophicum* in addition to preferentially aminoacylating the leucyl-O-tRNA. This high degree of sequence identity, in combination with the functional limitation and knowledge of O-RS secondary structure clearly defines what can be included in a genus of suitable O-RS molecules.

These amendments to claims 17 and 26 result in the O-RS species being defined in both functional and structural terms. Applicants assert that this amendment removes any perceived ambiguity regarding the definition of the O-RS species, and respectfully request that this rejection be withdrawn.

In the Office Action, the Examiner alleges that the term “conservative variant” as used in claim 18 to describe O-RS molecules finding use in the orthogonal translation systems of claim 17 encompasses O-RS sequences that may not function with the specified O-tRNA because conservative variants can include sequences having as little as 50% sequence identity.

Applicants disagree. The O-RS variants as recited in claim 18 are constrained by structural and functional limitations. These are (i) the O-RS must preferentially aminoacylate the O-tRNA, (ii) the O-RS comprises at least about 90% amino acid identity to a leucyl-O-RS of SEQ ID NO: 15 or 16, and (iii) the variants are conservative in nature, thereby preserving O-RS activity (see paragraphs 0050 and 0131-0133). In view of these constraints, applicants believe that the O-RS variants provided in claim 18 are sufficiently narrowly defined to find use in the O-tRNA/O-RS pairs.

35 U.S.C. § 102(b)

In the Office Action, claims 17-19 and 21-26 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by US Patent No. 7,083,970 to Schultz et al. The Examiner states that SEQ ID NOS: 4 and 5 of the present application are disclosed in US Patent No. 7,083,970. Applicants have amended claims 17 and 26 to remove recitation of SEQ ID NOS: 4 and 5.

Claims 17-26 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by WO2002/085923 to Schultz et al. The Examiner states that WO2002/085923 provides SEQ ID NO: 3 that is 100% identical to the leucyl O-tRNA of SEQ ID NO: 3 of the present application. Applicants point out what appears to be a clerical error in the Examiner’s rejection. WO2002/085923 provides SEQ ID NO: 3 that is 100% identical to the leucyl O-tRNA of SEQ ID NO: 5 (not SEQ ID NO: 3) of the present application. Applicants have amended claims 17 and 26 to remove recitation of SEQ ID NO: 5.

Claims 17-26 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by WO2002/086075 to Schultz et al. The Examiner states that WO2002/086075 provides SEQ ID NO: 3 that is 100% identical to the leucyl O-tRNA of SEQ ID NO: 4 of the present application. Applicants point out what appears to be a clerical error in the Examiner’s rejection. WO2002/086075 provides SEQ ID NO: 3 that is 100% identical to the leucyl O-tRNA of SEQ ID NO: 5 (not SEQ ID NO: 4) of the present application. Applicants have remove recitation of SEQ ID NO: 5 in the presently pending claims.

In the Office Action, the Examiner states that WO2002/086075 was made of record in the rejections that appeared in the previous Office Action. Applicants do not see where this international application is cited in the previous Office Action (although the content of that international application is identical to the disclosure of US 7,083,970, which is discussed in the previous Office Action).

In the present Office Action, the Examiner states that WO2002/086075 provides SEQ ID NO: 66 that is 100% identical to the leucyl O-RS of SEQ ID NO: 15 of the present application. Applicants point out what appears to be a clerical error in the Examiner's statement. WO2002/086075 provides SEQ ID NO: 65 (not 66) that is 100% identical to the leucyl O-RS of SEQ ID NO: 15 of the present application.

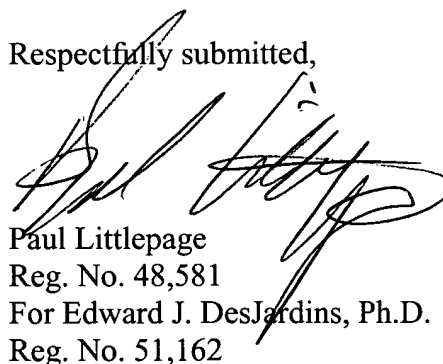
Applicants respectfully request that the rejection based on anticipation be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe that all claims now pending in this application are enabled and novel, and are in condition for allowance. The Examiner is encouraged to telephone Edward J. DesJardins to expeditiously resolve any further issues in order to put this case in condition for allowance

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- 1) A transmittal sheet; and
- 2) A receipt indication postcard.